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Altering The Cell— The Vistas Are Breathtaking

Last year some 200,000 babies were born in the United States with genetic defects ranging from a cleft lip to mental retardation. Can such inherited disorders be cured by chemically altering the genes? Can we, for instance, replace a defective gene with a good one?

This dramatic but visionary program — which has been gaining an increasing number of adherents in the last 10 years—took on added stature in the scientific community this month with the announcement in Nature, the eminent British scientific journal, that three American doctors had for the first time successfully introduced a foreign gene into a human cell and shown that it grows there—and that it may actually have changed the cell's genetic mechanism and hence the trait it will pass on to succeeding generations of cells.

In an ingenious series of test-tube experiments, Dr. Carl R. Merril of the National Institute of Mental Health, Dr. Mark R. Geier of George Washington University and Dr. John C. Petricciani of the National Institutes of Health in Bethesda, used skin cells from a patient suffering from galactosemia, a gene defect which prevents the victim's body from metabolizing ordinary milk. Normally this gene produces an enzyme in the blood stream that breaks down the milk sugar known as galactose so that it can be easily absorbed by the body. The newborn with galactosemia can become retarded, even die prematurely, if fed milk.

The scientists also made use of a virus called "Lambda phage," a package of genetic material which happens to include the missing enzyme-producing gene. Adding this virus to the defective human cell, they discovered that there was a marked increase in the cell's output of the enzyme. Conclusion: The bacterial virus had invaded the human cell, apparently altering some of its genetic material and leaving it with instructions to produce the vital enzyme needed to digest milk sugar.

Although there is no clear evidence yet of a permanent alteration of the cell, this finding is the latest—and, if confirmed by others, the most significant—step in a sequence that began in the late 1940's when scientists first became aware through bacterial studies that you can theoretically add a gene to a cell and control its heredity.

However, the practical path to chemical control of heredity in dealing with complex mammalian cells has been strewn with disappointment. Ten years ago a University of Wisconsin scientist named Waclaw Szybalski announced that he had injected a cell normally sensitive to a certain drug with a virus containing a built-in resistance to that drug; he indicated that the original cell had grown resistant to the drug. But he couldn't repeat his results, nor could anyone else.

Despite such discouragements, the fantastic growth through the 1960's of molecular biology continued to generate a high fever of excitement. Dr. Joshua Lederberg of Stamford University, the Nobel Prize-winning geneticist, first suggested the chemical replotting of human heredity 10 years ago—and was roundly criticized for proposing to do "God's business," as Jean Rostand put it. Today his ideas have found support among many of his colleagues. In fact, some have been applying Dr. Lederberg's concept of gene modification to a restructuring of humanity.

The most enthusiastic devotee of this "new eugenics" is Robert Sinsheimer of Cal Tech, a molecular biologist who seems to hold a transcendental vision of a greater human race achieved through controlled genetic change. A couple of weeks ago he told an international audience of social and physical scientists at the Institute of Society Ethics and the Life Sciences, a think tank at Hastings-on-Hudson, N. Y., that in gene manipulation man will find the prime mover in a never ending spiral of self improvement.

Such enthusiasm for the future of genetic engineering—and its entry to the shores of Avalon—is not universal among scientists. Indeed some doctors have become increasingly concerned about the undue romantic attention being paid to the potential of genetic manipulation not only in jazzing up the human race, but even in individual treatment. "I still have distinct reservations with regard to gene therapy," says Dr. John Littlefield, head of the genetic unit of the Massachusetts General Hospital, who last July co-authored a guest editorial on the subject for the magazine Science. "Only a small number of disorders of genetic origin could ever be amenable to such intervention and the risks are too great. Who can tell what strange side effects, infections or mutations might occur when you put alien genetic material inside the cell? I want to emphasize that gene engineering might be useful in the future but it is a longer way off than many would believe."

The consensus among medical men seems to be that diseases involving a single bad gene, where the biochemical pathway could be traced with assurance, might eventually be treated by building in new genes from outside sources. These diseases include phenylketonuria, an inherited nervous disorder that is now being alleviated by diet; the dread Tay-Sachs disease, a fatal destruction of the nervous system which mainly afflicts Jewish youngsters, and possibly sickle cell anemia, a blood disease which affects mainly blacks. On the other hand, diabetes and other more complicated genetic diseases which involve many as yet unidentified genes, or mongolism, which is caused by an extra chromosome (47 instead of 46) in the human heredity complement of the cells, are not yet likely candidates for clinical genetic manipulation. "Even in the case of galactosemia," adds Dr. Richard Roblin of Massachusetts General, "new genes would have to be injected into the right part of the body to be effective in getting into all the cells involved. We don't yet know how to do this without affecting other cells, perhaps dangerously."

Many scientists, however, see positive value emerging from the continuing knowledge of gene manipulation. Dr. Littlefield sees it as a powerful tool in research; it will help us, he says, in understanding the basis of disease on the molecular level. If the rate of progress in genetics continues, he adds, we might be able some day "to turn genes on and off at will—and that, of course, will be a real breakthrough in medical treatment."

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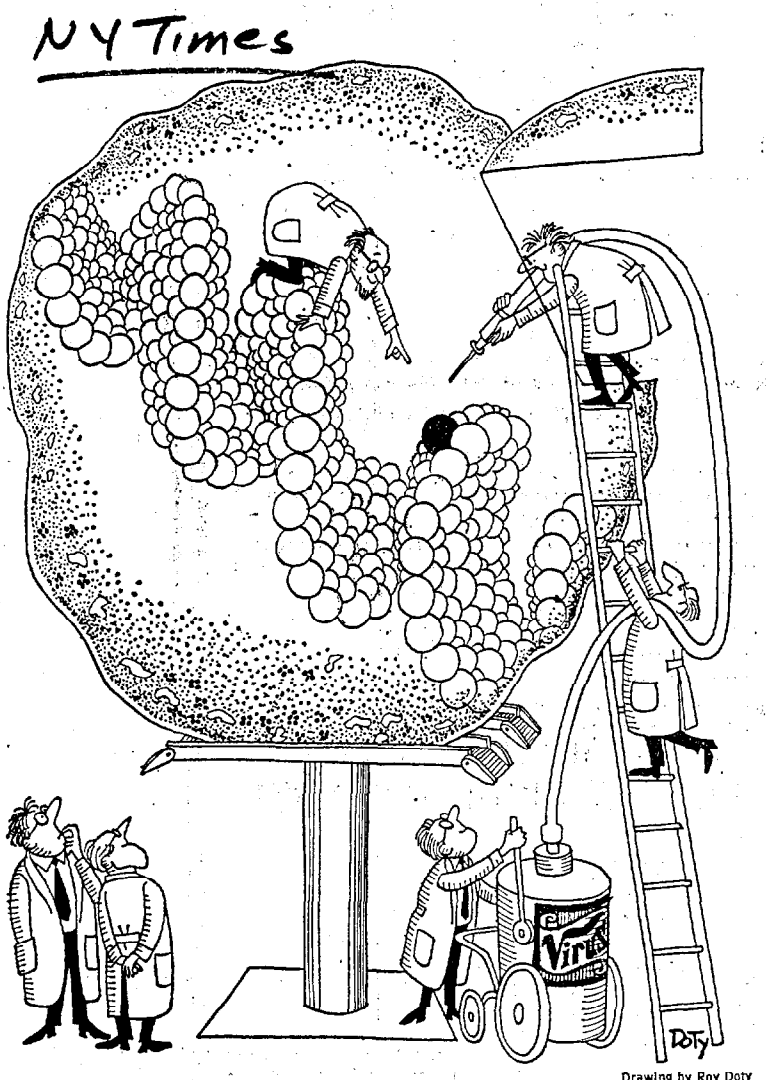

Drawing by Roy Doty

Genetic surgery to cure inherited disorders? Three American scientists have taken a step on that long road: They introduced a foreign gene into a cell (by way of a virus) and showed that it grew there and may actually have changed the cell's genetic mechanism.